Genetic Testing for Breast and Ovarian Cancer Risk

An Informational Guide

Penn's Cancer Risk Evaluation Program

University of Pennsylvania
CANCER CENTER
University of Pennsylvania Health System

Introduction

The University of Pennsylvania Cancer Center is studying breast and ovarian cancers that are strongly associated with family history. This booklet describes the cancer predisposition genes BRCA1 and BRCA2, the process for genetic testing, and how results may provide information for individuals and their families.

Breast and ovarian cancer risk sometimes runs in families. In this setting, there may be more family members with either breast and/or ovarian cancer than expected just by chance alone. In addition, in families with inherited cancer risk, people may be diagnosed with cancer at earlier ages than typically seen for that cancer. Families with inherited cancer risk are sometimes called "hereditary cancer families," since cancer risk can be passed from one generation to the next.

Throughout this booklet, words that might be new to you are shown in italics. Definitions for these and other terms related to cancer and genetics begin on page 24. Other resources about cancer, its treatment and living with cancer in your family are listed on pages 21 and 22.

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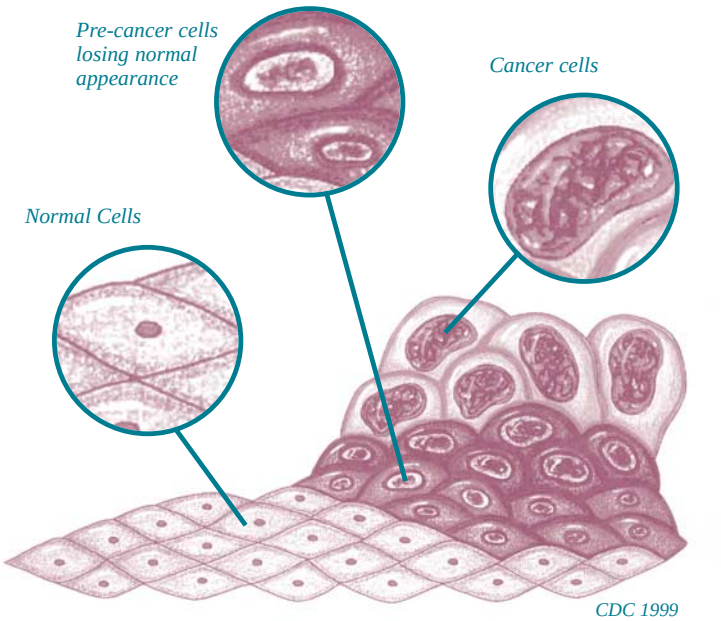
What is Cancer?

The human body is made of millions of individual cells. *Cancer* is a condition where certain cells in the body are no longer growing and dividing normally. Cancer cells may grow too quickly, and form a lump, or a *tumor*. When cancer cells are looked at under a microscope, they show certain distinct features. A pathologist, a physician specializing in the study of cells, can determine if they are cancerous. If cancer is present, a tumor is malignant. If cancer is not present, a tumor is considered benign.



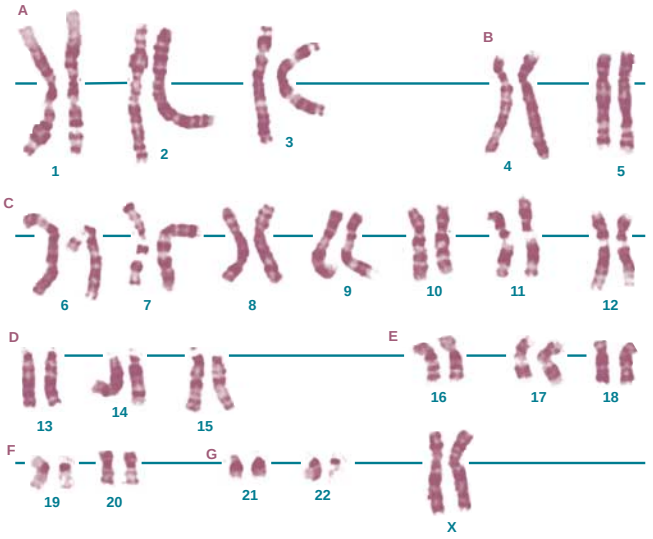
What are Genes?

Genes are the instruction manuals contained in all of our cells. Through the chemical code that makes up a gene, the body receives messages that control every body function. Most body functions, such as digestion, are complicated, and involve not just one but many genes. Genes also contain instructions for the physical make-up of the body. Certain genes may produce brown hair, while other genes send messages for blonde hair. When a gene is not working properly, it is said to be altered or mutated. A gene mutation may disrupt a normal body function.

We each have about 80,000 different genes. There are still many genes that have yet to be identified. While it is known that mutations in *BRCA1* and *BRCA2* can increase cancer risk, there are still more undiscovered genes that can also significantly increase breast and ovarian cancer risk.

Genes are arranged on structures in each cell called *chromosomes*. A chromosome may contain hundreds to thousands of genes, arranged like beads on a string. Each bead represents a gene. Humans have 23 pairs of chromosomes in each cell, with different genes located on different chromosomes. Chromosomes can be seen under a microscope (see below) and are numbered from pair 1 to pair 22, from biggest to smallest. One pair of chromosomes, called "X" and "Y," are the sex chromosomes, and have genes specific to male and female development. The BRCA1 gene is located on chromosome pair 17, while the BRCA2 gene is located on chromosome pair 13.

Female Human Chromosomes



How are Genes Related to Cancer?

Cancer development is a multistep, complex process. Cells receive many instructions about when to grow and divide, and when to stop growing. If certain genes are not working properly (mutated) then cells may not get the proper instructions about when to grow and divide. If the mutated gene plays a very important role in controlling normal cell growth, then cancer could develop. Cells can grow more quickly without the normal controls and form a tumor.

Most people develop cancer because of a series of gene mutations, environmental and lifestyle events that occur for multiple reasons over many years. All of us develop mutations in our genes as we age. Some of these gene mutations will be repaired, and some of these mutations will not. Most people with cancer are over the age of 50, since it takes time for these mutations to accumulate.

In families with hereditary forms of cancer risk, a mutation is present in a single, very important gene, and is present at birth in all cells in the body. A child may inherit this gene mutation from a parent. Inheriting a mutation in a gene that plays a very important role in controlling normal cell growth substantially increases cancer risk. However, these cancer risk genes in no way guarantee that cancer will develop; inheriting a mutation in a cancer risk gene, like BRCA1 or BRCA2 means only that your risk is higher than someone who does not carry such a mutation in their cells.

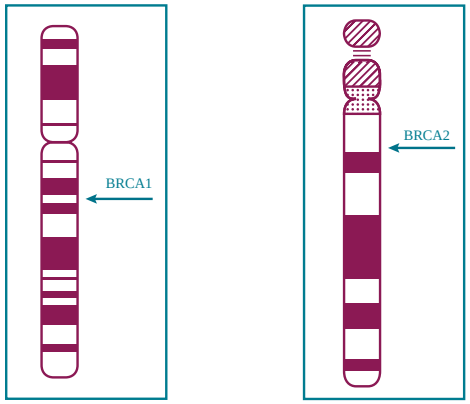
How much Breast and Ovarian Cancer Susceptibility is Hereditary?

Only about 5-10% of breast cancer, and 5-10% of ovarian cancer is strongly related to mutations in single strong cancer risk genes. Breast cancer is a common disease, affecting about 11%, or 1 in 9 women in the United States. Ovarian cancer is less common, affecting about 1-2%, or 1 in 70 women in this country. While most women will develop breast or ovarian cancer because of non-inherited mutations in many different genes, a small number will inherit a significant risk of developing these cancers because of a single BRCA gene mutation.

Features of Hereditary Cancer

In order to determine the chance that a mutation in a single, strong cancer risk gene is present, a complete family history, including at least three generations of relatives should be examined. The following features are associated with hereditary cancer:

- Multiple generations of people affected with the same or related cancers
- At least some people with cancer diagnosed at early ages for that cancer
- Some people in the family may have more than one type of cancer, like a woman with both breast and ovarian cancer



Chromosome 17 *Chromosome 13*

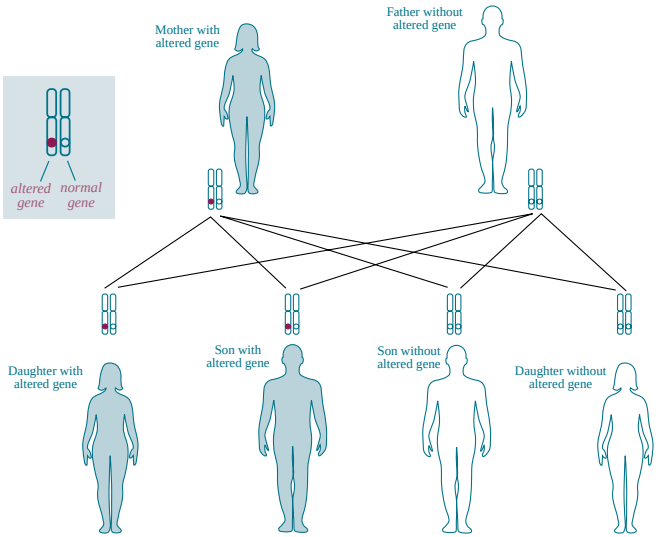
How Can Cancer Risk Run in a Family?

Genes are inherited from your parents. All genes are present in pairs. A father contributes half of a pair of a child's genes in the sperm and the mother contributes the other half of each pair in the egg. The fertilized egg will then have two copies of each gene.

Mutations in BRCA1 and BRCA2 are called *dominant mutations* (see chart, page 6). This is because having a mutation in only one copy of a BRCA1 or BRCA2 gene is enough to increase cancer risk. One can think of a gene as a page in an instruction manual for the cells of the

body. One gene in a pair may be mutated, but the other copy of this gene in the gene pair is normal and working properly. So, people with mutations in BRCA1 or BRCA2 are not born with cancer. However, such individuals are at increased risk of cancer because there is no back-up copy of this gene. There is no back-up page in the instruction manual for the body to refer to, should something go wrong.

A parent who has a mutation in BRCA1 or BRCA2 has a 50% chance of passing it on to their child, and a 50% chance of passing along the normal copy of the gene in that gene pair. Men as well as women can inherit and pass on a mutation in BRCA1 or BRCA2 to either a son or daughter. Each time someone has a child, the same 50-50 chance is present to either pass along the normal or mutated gene. Gene mutations in BRCA1 and BRCA2 do not skip a generation. A child who does not inherit a BRCA mutation from a parent cannot then pass a BRCA mutation to the next generation. A parent with a BRCA mutation may pass the mutation along to one, some, or none of his or her children.



Dominant Inheritance of Cancer Susceptibility

In this figure, the altered gene is represented by a dot on one of the chromosomes.

Cancer Risks Associated with BRCA1 and BRCA2

Learning about the presence or absence of a BRCA gene mutation can help guide medical care. A person with a gene mutation may benefit from more frequent check-ups and screening tests, starting at earlier ages, than someone who does not have a gene mutation. Recent research also suggests specific risk reduction measures may be effective for individuals with BRCA mutations. The cancer risks associated with BRCA1 and BRCA2 are presented as ranges, since cancer risk may vary in different families or population groups. At present, we can not predict where in the range any individual will fall. There are other genetic and lifestyle factors that can influence, or modify cancer risk associated with mutations in BRCA1 and BRCA2. Discovering these factors may help us provide a more accurate individual *risk assessment*.

Lifetime BRCA1 and BRCA2 Cancer Risks for Women

Type of Cancer	Women with BRCA1 mutation	Women with BRCA2 mutation	Average woman in US without mutation
Breast	50-85%	50-85%	11%
Ovarian	20-40%	10-20%	1-2%
Colon	Possibly increased	Possibly increased	5-6%
Pancreatic	1%	2-3%	1%

Lifetime BRCA1 and BRCA2 Cancer Risks for Men

Type of Cancer	Men with BRCA1 mutation	Men with BRCA2 mutation	Average man in US without mutation
Breast	0.1%	6%	0.1%
Prostate	30%	20-30%	17%
Colon	Possibly increased	Possibly increased	5-6%
Pancreatic	1%	2-3%	1%

People with mutations in BRCA1 or BRCA2 may develop one, none or several cancers. Those who have developed one cancer are at increased risk of developing another cancer. Unfortunately, being diagnosed with one cancer doesn't mean other cancer risks no longer apply. Women with BRCA mutations who have developed one breast cancer are at increased risk of developing a second breast cancer, as well as ovarian cancer.

Genetic Testing for Mutations in the BRCA Genes

When there is a significant chance of finding a mutation in a BRCA gene, some individuals choose to be tested to learn if they inherited a mutation. Testing is becoming more wide-spread among high-risk families as treatment recommendations are developed and insurance issues are resolved. Genetic testing is typically a blood test. *DNA*, the genetic material which contains all the genes, is isolated from blood cells, and studied for the presence or absence of inherited mutations in specific genes. One can think of genetic testing as a "spell-checking process" in which the letters of the genetic code in specific genes are studied for misspellings. Some misspellings are harmful, and are called mutations. Mutations in BRCA genes lead to an increased risk of breast and ovarian cancer.

Families at increased risk of having a BRCA1 or BRCA2 mutation may have:

- Several relatives with breast cancer, with some women diagnosed before the age of 50
- Ovarian cancer in one or more women
- Both breast and ovarian cancer diagnosed in the same woman
- A man with breast cancer
- Ashkenazi Jewish (Eastern European) heritage

Families found to have BRCA1 and BRCA2 mutations may have one, several, or none of these features. Through the genetic counseling process, a person learns how likely it is that a mutation is present. The only way to know for sure if a mutation is present is to do genetic testing. Testing is a complex and time consuming process for a laboratory.

Some insurance companies cover the cost of testing fully or partially, while others do not. It is possible to learn your own insurance company's policy regarding genetic testing and reimbursement so you will know the financial implications before making a decision about testing.

It is suggested that testing in the family start with someone who has had an early onset (before age 50) breast, ovarian or male breast cancer diagnosis. This is because such a person is most likely to have an inherited mutation, if a detectable mutation exists in the family. Until you know the source of cancer risk in a family, it is hard to know the significance of a negative result for those who are cancer free. If there is a different gene, perhaps an undiscovered one not yet available for testing, that underlies a family history of cancer, then a BRCA test result may not detect the most important indicator of risk in a cancer-free individual.

Sometimes it is not possible to start testing with an affected relative. A relative with cancer may either be unavailable or unwilling to be tested. Even in this situation testing can still be performed on someone not affected with cancer. Through the genetic counseling process, you will understand what testing strategy will be most informative for your family.

Making Decisions About Genetic Testing

Deciding whether or not to have genetic testing is a personal decision. In addition, **when** to have genetic testing should also be considered. For example, testing young adults may not be beneficial, since medical decision-making may not be affected for several years. Children are currently not candidates for BRCA testing, since there is no known cancer risk, or medical intervention that takes place during childhood, and testing may be psychologically difficult for children. In addition, all individuals should be given the chance to make their own decision about testing, and the vast majority of children are not prepared to do so independently.

Genetic testing is a personal decision, but learning about the presence of an inherited mutation that increases risk for cancer can also affect other family members, and possibly even family relationships. Other relatives could learn more about their cancer risk through testing a parent, brother, sister or cousin, for example, and this information may or may not be welcome. While we strongly encourage people to share genetic testing information with relatives, ultimately each family member will choose whether or not to be tested.

Benefits of Genetic Testing

Possible benefits of genetic testing include:

- Development of a treatment plan that is likely to reduce cancer risk in individuals who tests positive. This may include facilitating difficult medical decisions, like whether or not to have *prophylactic mastectomy* or *oophorectomy*.
- The opportunity to design a personalized cancer screening program, tailored to individual risk.
- Understanding the source of cancer risk in the family, and following the latest research on possible interventions.
- Making information available for adult children, and children as they become adults.
- Improved ability to cope with cancer risk, since the risk could be better defined and understood through genetic testing. Some individuals with a known mutation in their family will learn they did not inherit a gene mutation, and are not at high risk in spite of their strong family history of cancer. Some individuals will learn they did inherit a gene mutation, and will then have more information to alter their cancer risk management.

Drawbacks of Genetic Testing

Possible drawbacks of genetic testing include:

- The state-of-the-art genetic testing can not yet find all BRCA gene mutations. It is estimated that about 10% of all mutations are not detectable using the current state-of-the-art technology. The genetic counseling process should inform people about what the significance of a negative result (not finding a mutation) will be.
- The cost of testing may range from $250 - $2,600, and may or may not be covered by insurance. Information about insurance coverage can be obtained before testing decisions are made.
- The possibility that finding a genetic mutation could cause worry, anxiety or other emotional distress.
- The remote possibility of genetic discrimination for some people.

What Does a Negative Test Result Mean?

Regardless of a genetic testing result, it is important for people to realize that anyone can develop cancer, whether or not a cancer risk gene mutation is present. Most cancer in the general population is not a result of these inherited gene mutations. While a person who does not inherit a familial cancer-risk gene mutation has a much lower risk, the average person's risk is still present, and screening recommendations for the early detection of cancer risk for the general population still need to be followed.

Negative BRCA Results When A Family Mutation is Known

When someone has been tested, and a BRCA mutation has been found, then the source of cancer risk for the family is known. If other individuals in the family are tested and receive negative results, then these individuals are no longer at increased risk for developing BRCA-related cancers. This is a "true negative" result. If there is no other family history or significant risk factor, then such an individual may follow cancer screening recommendations from that point on for an "average" risk person, and not a high-risk person. In addition, an individual with a negative result cannot pass the family mutation on to his or her children.

Negative BRCA Results When a Family Mutation is Unknown

When no one in the family has been found to have a detectable BRCA mutation, negative test results need to be interpreted with caution. In this setting, a negative result may not really be negative. A cancer predisposing mutation may still be present in the family possibly in another gene. We know that mutations in the BRCA1 and BRCA2 genes do not explain all hereditary patterns of breast and ovarian cancer. A family may have a mutation in a different gene, perhaps not yet discovered and unavailable for testing. Unless there is a known mutation in the family, a negative result from BRCA testing does not exclude genetic risk for an individual.

Cancer Risk Management

A personalized cancer risk management program can be developed for individuals known to be at increased cancer risk due to a mutation in BRCA1 or BRCA2. A cancer risk management plan is typically tailored to a person's unique circumstances and preferences. You and your physicians will ultimately decide what plan makes the most sense for you. Cancer risk management generally includes the following categories:

- Intensive screening to optimize the chances of early detection, should cancer develop.
- Consideration of prophylactic or risk reducing surgical removal of ovaries and possibly breast tissue
- Chemoprevention - taking a medicine thought to lower the chances of developing cancer.

Screening

The University of Pennsylvania Cancer Center recommends the following screening procedures for women and men found to have a mutation in either BRCA1 or BRCA2.

The benefits of these screening procedures for individuals with BRCA mutations have yet to be proven, and so far are based on expert opinion only. However, removal of the ovaries has been shown to reduce both breast and ovarian cancer risk significantly. The types of studies needed to prove the benefits of these screening procedures may take years to become available, since researchers need to be able to follow individuals over time to see how these procedures affect long-term outcomes. Since BRCA1 and BRCA2 were only discovered in 1994 and 1995, follow-up time for those with mutations has been limited. However, the rationale for these screening recommendations is based on the known importance of early detection for cancer. Generally, cancer that is detected in earlier stages is more easily treated, and outcomes are often more favorable.

Screening for Women with Mutations in BRCA1 or BRCA2

Type of Cancer	Screening Procedure	Starting Age	Frequency
Breast	Mammograms	25 years	Every 6-12 months
	Physician Breast Exams	25 years	Every 6 months
	Breast Self Exam	20 years	Once every month
Ovarian	CA-125 blood test Ovarian ultrasound *Note: these tests have never been proven to reduce the risk of dying from ovarian cancer.*	25 years, until childbearing complete, then removal of ovaries (prophylactic oophorectomy)	Every 6-12 months
Colon	Colonoscopy	50 years	Every 3-5 years

Screening for Men with Mutations in BRCA1 or BRCA2

Type of Cancer	Screening Procedure	Starting Age	Frequency
Breast	Physician Breast Exams	50 years	Once every year
Prostate	Prostate Exam and PSA blood test	45 years	Once every year
Colon	Colonoscopy	50 years	Every 3-5 years

Research Screening Options

There are multiple research studies currently being conducted at the University of Pennsylvania Cancer Center and other centers specifically for individuals at high risk of developing cancer. It is hoped that these studies will find even more sensitive ways to follow high-risk individuals. Current screening opportunities for which you are eligible will be discussed with you as part of your genetic counseling sessions.

Surgical Options for Women with BRCA1/2 Mutations

Prophylactic Mastectomy

At the present time, prophylactic mastectomy is the most aggressive prevention strategy available. We do not believe anyone needs to have this procedure, however, women found to be at very high risk of developing breast cancer may choose this option. Prophylactic mastectomy involves removing currently healthy breast tissue in the hopes of reducing breast cancer risk. While there has been controversy and debate regarding the effectiveness, studies have shown that this procedure reduces breast cancer risk by as much as 90% in women with a strong family history of breast cancer. We believe that breast cancer risk may be significantly lowered by this procedure, but studies are ongoing to more definitively answer this question in women with BRCA mutations.

One concern about prophylactic mastectomy arises because even the best surgical techniques do not allow the complete removal of all breast tissue in prophylactic simple mastectomy. Individuals who have inherited a mutation in a breast cancer susceptibility gene will have this mutation in every cell in the breast. For this reason, total mastectomy, and not subcutaneous mastectomy, (which removes less breast tissue), is recommended for women considering prophylactic surgery. For women considering this option, it is often helpful to consult with a plastic surgeon to learn about options for breast reconstruction. We encourage all women who would consider this option to take the time they need to make a thoughtful decision.

Prophylactic Oophorectomy

We now recommend removal of a woman's ovaries (oophorectomies) after childbearing has been completed. Recent studies suggest this approach will reduce ovarian cancer incidence by as much as 90%. However, some women will still develop cancer of the lining of the abdomen, a disease that behaves like advanced ovarian cancer. In addition to markedly reducing ovarian cancer risk, it appears that removing the ovaries from pre-menopausal women also reduces breast cancer risk by 50-60%. Therefore, the overall benefit of this surgery appears to be very significant. This is important since screening for ovarian cancer is very limited and usually does not detect ovarian cancer in the early stages.

Removing healthy ovaries in a post-menopausal woman will have no impact on her symptoms of *menopause*. Once a woman is post-menopausal, and has not had a period for at least a year, her ovaries no longer function to produce *estrogen*.

Prophylactic oophorectomy in pre-menopausal woman

Removing the ovaries in a pre-menopausal woman will cause her to enter menopause, since the ovaries provide a woman with her major source of estrogen. Because of this, prophylactic oophorectomy is typically only considered after a woman is sure she has completed her family. In addition, ovarian cancer risk becomes more significant for women in their 40s, 50s and beyond. Even in women with BRCA mutations, it is very uncommon to be diagnosed with ovarian cancer before the age of 40.

Hormone Replacement Therapy (HRT) for Pre-menopausal Women after Prophylactic Oophorectomy

While prophylactic oophorectomy reduces ovarian and breast cancer risk, there are additional health issues that need consideration. Estrogen provides women with major protection from bone loss, (osteoporosis), a condition where the bones are weakened and more easily fractured. In addition, estrogen provides women with significant protection from heart disease. Pre-menopausal women who undergo prophylactic oophorectomy may also experience some uncomfortable effects of menopause, such as hot flashes, vaginal dryness, mood swings and sleep disturbances.

Although studies are still underway, women with BRCA mutations who do not have breast cancer may choose to take *hormone replacement therapy (HRT)* after having their ovaries removed until around the time of natural menopause – age 50-55. This is because the replacement dose is lower than the dose of estrogen that would be produced by the ovaries if not removed. Thus even with HRT, removal of the ovaries results in a significant decrease in estrogen exposure.

The benefits of taking estrogen include prevention of osteoporosis and early heart disease, as well as control of post-menopausal symptoms such as vaginal dryness, hot flashes and sleep disturbances.

At age 50, it is recommended that women with BRCA mutations switch to *raloxifene* or *tamoxifen* or another medication in order to prevent excessive bone loss without prolonging estrogen exposure beyond the age of natural menopause. *Tamoxifen* (see page 18) or *raloxifene* (see page 17) can be started earlier (instead of HRT) if menopausal symptoms are not a problem. We recognize that many women at high risk of breast cancer will feel anxious about estrogen, and some choose not to do so. Discussions with the faculty of Penn's Cancer Risk Evaluation Program as well as with your personal physician are usually helpful in making these difficult decisions.

Hormone Replacement Therapy in Post-Menopausal Women with BRCA1/2 Mutations

Multiple studies have demonstrated a small increase in the risk for breast cancer in women who use post-menopausal HRT for more than five years. For this reason, post-menopausal women with mutations in a BRCA gene should consider alternatives to traditional HRT. These alternatives, including tamoxifen and raloxifene (discussed further below), will not help symptoms of menopause, such as hot flashes. Sometimes, women consider going on short-term HRT, and are then gradually weaned off as their symptoms permit. While there are no long-term studies to support or discourage use of HRT by post-menopausal women with mutations in a BRCA gene, this is the most cautious approach at present. Women with a previous breast cancer diagnosis are also typically discouraged from using traditional HRT.

Raloxifene: A Hormone Replacement Therapy Alternative

Raloxifene (also called Evista) is a *selective estrogen receptor modulator* (SERM) that has been shown to have positive estrogen-like effects on bone density and cholesterol levels. However, raloxifene has been shown to block the actions of estrogen on the breasts and uterus, and therefore, is not associated with an increase in risk for these cancers. Raloxifene has been shown to be effective in preserving bone density in post-menopausal women, and is currently being used for this purpose.

Raloxifene may also have positive effects on the risk for heart disease. While raloxifene does lower the levels of certain types of cholesterol (LDL – the "bad" cholesterol), and increase the level of HDL (the "good" cholesterol), these effects have not yet been shown to be as protective from heart disease as traditional estrogen replacement therapy. There is also some preliminary information that raloxifene may actually significantly lower the risk of developing breast cancer. Raloxifene may be associated with a slight increase in the risk of blood clots, including *pulmonary emboli* (a small blood clot in the lung) in older women, so the risks versus benefits of this medicine need to be carefully considered.

There will soon be additional alternatives to traditional HRT for post-menopausal women. It is important for a woman to discuss with her physicians all the current options and alternatives to traditional HRT in light of all of her personal risk factors before reaching a decision.

Chemoprevention

Chemoprevention, taking a medicine in an attempt to lower cancer risk, can provide additional choices for high-risk women. Tamoxifen is another SERM that has been used for over 20 years to treat women with breast cancer. Usage also is associated with reduced numbers of breast cancer occurrences in the opposite breast. A national study of over 13,000 healthy women at increased risk was completed, and determined that tamoxifen can lower the risk of developing breast cancer by 49%. This finding was felt to be very significant, and tamoxifen is the first FDA approved medication now available that has been shown to lower breast cancer risk in healthy women. No information is available yet on the number of women with BRCA

mutations in this study, but other preliminary studies now suggest that tamoxifen will lower breast cancer risk significantly for these women too. Tamoxifen was also associated with some protection from bone loss. Drawbacks to taking tamoxifen include a small risk for early stage uterine cancer, and a small increase in the risk for pulmonary embolism (a blood clot in the lung) and deep vein thrombosis (a blood clot in a major vein).

It is likely that eventually there will be multiple medications available for chemoprevention in those with mutations in BRCA1 and BRCA2. It is important to know all current alternatives, including the risks and benefits of each, before making a decision about chemoprevention.

When a new medicine for chemoprevention is tested to determine how much cancer risk can be reduced, it is generally offered as part of a clinical trial. These trials generally select participants to receive one of at least two medications. People found to have mutations in BRCA genes should be informed about all the chemoprevention trials that are available, including the risks and benefits, before deciding about this option. Participation in these trials is strongly encouraged.

Implications for Health and Life Insurance

Some people considering genetic testing are concerned about the possibility of genetic discrimination, for health and life insurance. Although there are many activists, including representatives from the University of Pennsylvania Cancer Center, working with groups to protect people from genetic discrimination, it is still an uncommon occurrence, and your risk of discrimination largely depends on your personal situation.

Individuals who have been diagnosed with cancer in the past should not be at any increased risk of discrimination beyond their previous diagnosis. And, just as insurance companies do not drop coverage for someone who develops cancer, there has not been an example of an insurance company dropping someone or raising the rates of someone who is found to have genetic susceptibility to cancer.

Most Americans get their medical insurance through their employer, as part of a group. Even people who have their own businesses often join with a group to buy into a medical insurance plan. A group health plan can offer any type of available insurance, such as

Blue Cross/Blue Shield, HMO insurance, or contract with any plan it chooses. A federal law enacted in 1997 (the Health Insurance Portability and Accountability Act, or HIPAA) makes it illegal to single someone out in a group health plan for higher or lower payments for their medical insurance based on genetic test results. The same federal law makes it illegal to drop a person, exclude someone, or deny any medical treatment, including treatment for cancer, by saying the person has a pre-existing condition.

The HIPAA law applies as long as a person maintains continuous group health insurance coverage with the same, or with a new group health insurance plan. Therefore, people who change jobs do not need to fear being denied access to the new group health plan policy. The policy can be through an employer, or any group, such as a trade group, or retired persons group such as AARP.

People who have group insurance are usually not underwritten. The process of underwriting is when someone tries to determine what a person may actually cost to insure. Most people are underwritten for car insurance, when you are asked how many accidents you've had, your age, gender, and where you live. Each of these things can affect your rates. Underwriting for health insurance may include questions about weight, smoking, and the presence of significant medical conditions like heart disease or cancer. If you signed up for medical insurance without filling out a detailed medical questionnaire, then you were not underwritten. And, if you were not underwritten, your past medical history, including your risk of cancer or results of genetic testing, will not be considered when setting the rate you pay for medical insurance. People with government sponsored insurance such as Medicare and Medicaid are not underwritten – only their eligibility to receive this benefit is considered.

A relatively small number of Americans purchase their own individual insurance plan, outside a group. They are not protected through the same federal law that protects those in group health plans. However, there are many states that have individually enacted laws to prevent genetic discrimination, whether you are in a group or private plan. There are only a handful of documented cases of genetic discrimination in this country, and although no one should be discriminated against based on valuable health information, many people assume that this risk is higher than we believe it to be.

Implications for Life Insurance

Since most people are underwritten for life insurance, a personal or family history of cancer, with or without genetic testing, could theoretically affect your rates. Although most life insurance companies do not ask about genetic testing, this could change in the future. Some people choose to purchase life insurance before undergoing genetic testing. The few cases of people being charged more or denied access to life insurance have been based on family history information, and not based on results from genetic testing. In each of these cases, women were able to get the policy they desired through a different company.

Employment Discrimination

Employment discrimination is an unfortunate risk in America, since some employers single people out with any medical condition that may affect how much an employee could cost a company, or how many days off work they may need. For example, an employer may believe that a person with a prior history of cancer is at risk of being absent more, and choose to promote someone else over this person, even if they are similarly qualified. For this reason, we suggest not discussing medical information, including information about genetic testing in the workplace. It is hard to know how common this practice is, since it is rarely reported.

Anyone who believes they have been discriminated against due to genetic information (family history of cancer, or genetic testing information) should call us at 215-898-0247, since the University of Pennsylvania Cancer Center is working closely with legal and policy advocates that may be able to assist in such a situation.

Future of Cancer Genetics Research

A committed search is underway to locate and identify additional genes associated with inherited susceptibility to cancer. It is difficult to know how quickly these discoveries will occur, since the research is extremely time consuming and labor-intensive. We are very grateful to the families who have participated in research studies aimed at identifying and understanding genes associated with familial cancer, as they have made it possible for this research to go forward. Their contributions have been critical in the identification of the BRCA genes, and continued contributions will help researchers better understand how to best manage inherited cancer risk. The ultimate goal of this research to better understand cancer, so that cancer treatment will be improved, and ultimately cancer can be prevented.

Resources

Many resources are available in the community to provide information about cancer. The following list should serve as a basic guide; more specific information may be available through these and other organizations.

University of Pennsylvania Cancer Center

The University of Pennsylvania Cancer Center is one of a select group of cancer centers in the nation approved and designated by the National Cancer Institute as a **Comprehensive Cancer Center**.

Cancer Center Programs

Breast and Ovarian Cancer Risk Evaluation Program: 215-898-0247

Penn's Cancer Risk Evaluation Program is for anyone who wants more information about personal risk for breast and ovarian cancer.

GI Cancer Risk Evaluation Program: 215-662-4740

This program provides specialty services to individuals and families concerned about risk for colon and other gastrointestinal cancers. Concern may arise because of a family member with cancers in the gastrointestinal tract, or because or a personal history of polyps in the GI tract.

Medical Genetics: 215-662-4740

Penn's Division of Medical Genetics offers specialty services for families with inherited susceptibility to all other forms of cancer, including prostate cancer, von-Hippel Lindau, Multiple Endocrine Neoplasia (MEN), and Li Fraumeni syndrome.

Toll-free Information Service: 1-800-789-PENN
The University of Pennsylvania provides the latest information about cancer — quickly and easily — through a single phone call. Call to ask questions about cancer and request free brochures. You can also get information about other resources and additional publications through this service.

OncoLink®
OncoLink is the University of Pennsylvania Cancer Center's award winning resource on the Internet. You can access OncoLink at *http://www.oncolink.upenn.edu*

Organizations

American Cancer Society (ACS): 1-800-ACS-2345
The ACS is a national, non-profit organization that supports research and educational efforts, as well as many local support groups. The ACS website can be reached at *http://www.cancer.org*

National Cancer Institute (NCI): 1-800-4-CANCER
The National Cancer Institute is a government organization that supports research and education, and has a vast amount of information about cancer diagnosis, treatment, clinical trials and cancer genetics. The NCI also maintains an informative website, reachable at *http://www.nci.nih.gov*

National Human Genome Research Institute (NHGRI)
For further information about genetics public policy, including information on health insurance and workplace legislation, visit their website at: *http://www.nhgri.nih.gov*

Susan G. Komen Breast Cancer Foundation: 1-800-462-9273
This national organization sponsors research, education and the annual "Race for the Cure" held in 109 cities across the country. Further information about the Komen Foundation is available at *http://www.komen.org*

The Wellness Community
(Philadelphia and Bucks County Branches): 215-879-7744
The Wellness Community offers, free of charge, psychological and emotional support, educational workshops, exercise, stress management and social activities for people with cancer and their families.

Y-Me: 1-800-221-2141
This national organization sponsors a hotline, counseling, educational programs and self-help meetings for breast cancer patients, their friends and families.

Glossary

Alteration: A change in the normal sequence or chemical spelling of DNA, the genetic material. An alteration in DNA may also be called a mutation.

BRCA1 and BRCA2: The names for the first two genes to be discovered that increase risk for breast and ovarian cancer.

Cancer: A term for more than 100 disease that have in common the uncontrolled, abnormal growth of cells. Cancer cells can spread through the blood stream and lymphatic system to other parts of the body.

Chromosome: A threadlike structure that contains genetic information. There are 46 chromosomes in the human body, made up of 23 chromosome pairs.

DNA: Deoxyribonucleic Acid-the threadlike substance in every cell containing the genes, or hereditary information.

Dominant (Trait): Those conditions that are expressed in individuals when one member of a gene pair is altered and the other is normal.

Estrogen: A hormone produced by the ovaries associated with female characteristics. Women produce estrogen in their ovaries from the time they begin menstruating (having periods) to the time they reach menopause (stop having periods). A small amount of estrogen is also produced by the adrenal glands. Estrogen also protects women from heart disease and bone loss.

Gene: An individual unit of hereditary information that is located at a specific position within the chromosome. A gene provides coded information for a specific characteristic, trait or body function.

Hormone Replacement Therapy (HRT): Prescription medication taken by women who are menopausal (no longer have periods) that may include a form of estrogen and/or progesterone. HRT may be taken to protect from heart disease and bone loss, and to minimize symptoms of menopause.

Mastectomy: The surgical removal of a breast.

Menopause: The permanent absence of periods of menstruation in a woman. Menopause may occur naturally as a woman ages, or due to surgery or medication such as chemotherapy for cancer.

Mutation: A change in the normal sequence or chemical spelling of DNA, the genetic material.

Prophylactic: Risk reducing treatment, such as surgical removal of healthy tissue in the hopes of preventing cancer.

Pulmonary Embolism: A blood clot in the lung.

Oophorectomy: Surgical removal of a woman's ovaries.

Raloxifene: A selective estrogen receptor modular (SERM) used to treat osteoporosis. Raloxifene may reduce breast cancer risk, although this effect is not yet proven. Raloxifene is also called Evista, and is used by some post-menopausal women as an alternative to traditional hormone replacement therapy.

Risk Assessment: The process of assessing personal medical and family history to determine the chance that cancer could develop.

Selective Estrogen Receptor Modulator (SERM): A class of medications sometimes used as alternatives to traditional estrogen replacement for post-menopausal women. SERMs have some of the benefits of estrogen, such as protection of bone density, but in some cases may have fewer risks.

Tamoxifen: A medication used to treat breast cancer, as well as lower breast cancer risk in high-risk women.

Tumor: An abnormal mass of tissue, which may be malignant or benign.

Notes

Cancer Risk Evaluation Program

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